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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: JOHN C. CHABALA et al

Group: 124

Serial No.: 928,111

Case No: 16112IA

Examiner:

Filed: 7/31/78

For: SELECTIVE HYDROGENATION PRODUCTS OF  
C-076 COMPOUNDS AND DERIVATIVES

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Commissioner of Patents & Trademarks  
Washington, D. C. 20231

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DISCUSSION OF PRIOR ART

Sir:

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The following references may be of interest  
to the Examiner in the examination of the above-  
identified application.

U.S. Patent 3,950,360 to Aoki et al  
U.S. Patent 3,853,842 to Kishi et al

Chemical Abstracts 86 (1977) 42838k

Tetrahedron Letters 10 pg. 711-714 (1975) Mishima et al

Journal of Antibiotics 29 (6) (1976) pgs. 76-34 to 76-42  
and 76-14 to 76-16.

Copies of the foregoing references are supplied  
herewith for the convenience of the Examiner.

R E M A R K S

The Aoki et al, Tetrahedron Letters and Journal of Antibiotics references were cited by Applicants in the parent application (USSN 838,603) to the instant application. The relevance of such references was discussed in Applicants Discussion of Prior Art filed in USSN 838,603 on December 8, 1977. A copy of said Discussion of Prior Art is enclosed herewith.

The other two references, Kishi et al and Chemical Abstracts were cited in the Official Action of August 25, 1978 in said parent application. Such references were used as the basis for a rejection of the process claims, the Examiner noting that Kishi discloses macrolides which are unsaturated and converted to the saturated version and the Chemical Abstract reference disclosing the use of Wilkinsons catalyst for the reduction of double bonds.

It is respectfully noted that such a rejection contains a rather simplistic analysis of the instant hydrogenation reaction. The Kishi et al compounds, while being macrolides, as noted by the Examiner, are vastly different from the instant macrolides. The Kishi starting compounds contain one unsaturation; the instant starting compounds contain five unsaturations. The Kishi et al starting compounds have the unsaturation in the large (15 membered) ring and said unsaturation is straddled by a hydroxy group and an epoxide group; the instant starting compounds have the unsaturation which is being reduced in a 6 membered spiroketal ring and said double bond has no reactive groups adjacent thereto. The Kishi et al reaction reduces the 10,11 unsaturation accompanied by the simultaneous reduction of the 12,13 epoxide; the instant reaction in spite of the presense of four other unsaturations is not accompanied by any side reactions.

Thus, it is clearly apparent that the Kishi et al reference and the Chemical Abstracts reference do not disclose any reaction conditions which would enable one skilled in this art to selectively reduce the C-076 22, 23-unsaturation without affecting any other reactive substituent. The catalytic reaction conditions in Kishi et al would not have afforded the single 22,23 dihydro compound of the instant invention, rather other double bonds would have been affected.. Also there is nothing in Chemical Abstracts which would indicate that the catalyst would have been able to selectively reduce one double bond out of five.


Thus, the Kishi et al and Chemical Abstract references do not anticipate or render obvious any of the instant claims.

It is further noted that the above characteristics of the starting materials for the instant compounds tend to demonstrate the unobviousness of the instant compounds themselves. One skilled in the art in examining said C-076 starting materials could not predict how to prepare the compound with one specific double bond reduced, and it would be equally impossible to predict the outcome of a hydrogenation reaction on the C-076 starting materials. The molecule is so complex, with such a varied group of reactive substituents, that a hydrogenation process could have many varied effects. The instant compounds are unique and it is submitted that said

compounds are patentable in view of the cited prior art.

Respectfully submitted,

By



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mah  
October 4, 1978  
Enclosure

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on the date appearing below.

MERCK & CO., INC.

By



Date 10/4/78  
David L. Rose